

## REMARKS

Claim 1 has been amended. Claims 2, 3, 9-11, and 17 have been cancelled. Claims 1, 4-8 and 12-16 are pending in the instant application.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance.

### **I. The Rejection of Claims 1-8 under the Doctrine of Obviousness-Type Double Patenting**

Claims 1-8 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application Serial No. 10/463939.

Applicants have abandoned Application Serial No. 10/463939 rendering the rejection moot.

### **II. The Rejection of Claims 1, 2, 4-6, 8, and 16 under 35 U.S.C. § 102(b)**

Claims 1, 2, 4-6, 8, and 16 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Bracke *et al.* (U.S. Patent No. 4,517,295). The Office Action stated:

Bracke *et al.* teach a method of purifying hyaluronic acid from bacterial culture. As part of the process of producing hyaluronic acid, the bacteria are grown in a fermentation broth comprising the divalent salts calcium chloride and magnesium sulfate, reading on the limitation that the method of instant claim 1 comprises adding a divalent salt to the the [sic] fermentation broth, as well as instant claim 6, which limits that divalent salt to magnesium or calcium (see col. 2, lines 45-65, for example). The method taught by Bracke *et al.* comprises growing *streptococcus* bacteria in a fermentation broth. This *streptococcus* species naturally produces hyaluronic acid and secretes it into its growth medium (see col. 2, lines 5-34, for example). The cells are then flocculated and separated from the fermentation broth which contains the desired hyaluronic acid (see col. 3, lines 32-45, for example). Specifically, *streptococcus* is a prokaryote, reading on claim 2. The hyaluronic acid produced by this method has a molecular weight of 55,000 (see col. 1, lines 48-60, for example). Once flocculated, the bacteria are removed by a filtration process (see col. 3, lines 46-51, for example). Flocculation of the *streptococci* is achieved in part by addition of trichloroacetic acid, reading on the limitation of instant claim 16 that one more flocculating agent is added to the fermentation broth (see col. 3, lines 32-45, for example). Therefore the teachings of Bracke *et al.* are deemed to anticipate the instant claims 1, 2, 4-6, 8, and 16.

This rejection is respectfully traversed.

Under the standard required for anticipation under 35 U.S.C. § 102, the cited prior art reference is required to disclose every element of the claimed invention. *Lewmar Marine Inc. v. Barient Inc.*, 3 USPQ2d 1766 (Fed. Cir. 1987).

Claim 1 has been amended to incorporate the limitation of claim 3.

Bracke *et al.* disclose a method for flocculating a *Streptococcus* fermentation broth with trichloroacetic acid.

However, Bracke *et al.* do not disclose a method of flocculating *Bacillus* cells and/or removing high molecular weight contaminants from a fermentation broth, comprising adding a divalent salt to the fermentation broth comprising a glycosaminoglycan of interest after which the *Bacillus* cell and/or the high molecular weight contaminants are removed, wherein said *Bacillus* cell produces the glycosaminoglycan of interest, as claimed herein. Moreover, Bracke *et al.* do not disclose the addition of a divalent salt to a fermentation broth to flocculate *Bacillus* cells and/or remove high molecular weight contaminants from the fermentation broth.

Since Bracke *et al.* do not disclose every element of the claimed invention, Applicants submit, therefore, that the rejection under 35 U.S.C. § 102 has been overcome and respectfully request reconsideration and withdrawal of the rejection.

### III. The Rejection of Claims 1, 2, 4-6, 8, and 16 under 35 U.S.C. § 103(b)

Claims 1, 2, 4-6, 8, and 16 stand rejected under 35 U.S.C. § 102(b) as being unpatentable over Weigel *et al.* (WO 99/23227) in view of Kanani *et al.* (U.S. Patent No. 3,878,093). The Office Action stated:

A person of ordinary skill in the art at the time the invention was made would have been motivated to add divalent salt, change the pH of the fermentation broth, and heat the fermentation broth, because Weigel *et al.* teach that *Bacillus* can be induced to secrete hyaluronic acid into their fermentation broth, and that it is desirable to separate the bacteria from their fermentation broth, and Kanani *et al.* teach a method of producing strong, easily separated flocs by changing pH and temperature of the fermentation broth that allows for the easy purification of hyaluronic acid demanded by Weigel *et al.* Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to employ the flocculation method of Kanani *et al.* in a method of producing and purifying hyaluronic acid taught by Weigel *et al.*

This rejection is respectfully traversed.

The Examiner has the initial burden of establishing a *prima facie* case of obviousness. A finding of obviousness under § 103 requires a determination of the scope and content of the prior art, the differences between the claimed invention and the prior art, the level of ordinary skill in the art, and whether the differences are such that the claimed subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383 US 1 (1966). Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion that the combination be made. *In re Stencel*, 828 F2d 751, 4 USPQ2d 1071 (Fed. Cir. 1987).

A patent claim is obvious over a combination of prior art references only when "the prior art would have suggested to one of ordinary skill in the art that [the claimed invention] should be carried out and would have a reasonable likelihood of success... . Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Dow Chemical*, 837 F.2d 469, 473 (Fed. Cir. 1988); see also, 35 U.S.C. §103. An invitation to experiment, alone, cannot make an invention obvious. *In re Dow*, 837 F.2d at 473.

Weigel *et al.* teach recombinant methods of producing hyaluronic acid in bacterial cells. Moreover, Weigel *et al.* teach that cells can be separated from a fermentation broth by the addition of trichloroacetic acid to flocculate the cells and associated debris (page 63, lines 17-23). However, Weigel *et al.* do not teach or suggest the addition of a divalent salt as a flocculating agent to a fermentation broth to flocculate *Bacillus* cells.

Kanani *et al.* teach a method for separating bacterial cells from an aqueous medium wherein the cells are flocculated, by subjecting the medium to at least one of the steps of (A) raising the pH of the medium to a value within the range 8 to 11 by treatment with an alkali, and (B) heating the medium to a temperature within the range 50°C to 200°C; followed by the step of lowering the pH to a value within the range of 2 to 5 by treatment with an acid, and separating the flocculated cells from the medium. Kanani *et al.* also teach that when the alkali treatment of step (A) is employed, the pH is preferably raised to a value within the range 8 to 9, but if the heating treatment of step (B) is omitted, a higher pH is preferred, e.g., 9 to 11. For raising the pH within the range 9 to 11, Kanani *et al.* suggest that sodium hydroxide is preferred for raising the pH, but other alkaline compounds may be used including potassium hydroxide and calcium hydroxide. However, Kanani *et al.* do not teach or suggest the addition of a divalent salt as a flocculating agent to a fermentation broth to flocculate *Bacillus* cells.

Weigel *et al.* and Kanani *et al.*, alone or in combination, do not teach or suggest a method of flocculating *Bacillus* cells and/or removing high molecular weight contaminants from a fermentation broth, comprising adding a divalent salt as a flocculating agent to the fermentation broth comprising a glycosaminoglycan of interest after which the *Bacillus* cell and/or the high molecular weight contaminants are removed, wherein said *Bacillus* cell produces the glycosaminoglycan of interest, as claimed herein.

The Office asserts that Kanani *et al.* teach that flocculation can be achieved by addition of calcium hydroxide. Applicants respectfully disagree with the Office's assertion. Kanani *et al.* teaches a method of flocculating cells by raising the pH of the medium to a value in the range 8 to 11 by treatment with an alkali such as sodium hydroxide, potassium hydroxide, or calcium hydroxide. There is no teaching or suggestion by Kanani *et al.* of using a divalent salt as a

flocculating agent to flocculate *Bacillus* cells.

Applicants submit, therefore, that it would NOT have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add a divalent salt to flocculate *Bacillus* cells in the recovery of a glycosaminoglycan of interest and respectfully request reconsideration and withdrawal of the rejection.

#### IV. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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